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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,725	02/04/2004	Christophe Alain Thuriiau	00537-178003	4960

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EXAMINER
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TUCKER, ZACHARY C

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 04/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/771,725	THURIEAU ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Zachary C. Tucker	1624	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 April 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,5-20 and 30-36 is/are pending in the application.
- 4a) Of the above claim(s) 5-8,10,12-20 and 30-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☒ Claim(s) 9 and 11 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>5Apr06</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of amendments to the claims, a Terminal Disclaimer over copending application serial number 10/333,556 and an Information Disclosure Statement, all filed 5 April 2006 have been entered.

### ***Response to Amendment***

As requested in the correspondence from applicants, filed 5 April 2006 (hereinafter "present amendment"), which is in reply to the Final Rejection mailed 5 October 2005 (hereinafter "previous Office action"), claims 1, 9, 10, 17 and 19 have been amended and claims 2-4, 21-29 and 37-43 have been cancelled.

### ***Election/Restrictions***

Claims 31-36 remain withdrawn from consideration, as being drawn to a nonelected invention, as the conditions for rejoinder have not been satisfied (the elected Group is not in condition for allowance). Claims 5-8, 10 and 12-20 remain withdrawn from consideration because although the previously stated rejection of claim 1 under 35 U.S.C. 102(b) has been overcome by virtue of the present amendment, the search was expanded and art anticipating claim 1 was found, whereupon the searched was

stopped. Instant claim 1 has not been completely searched. Claims 9 and 11 have been completely searched. Claims under examination are 1, 9 and 11.

NOTE: The PTOL-326 form ("Office Action Summary") accompanying the previous Office action erroneously indicated that 2-8 and 10-43 were withdrawn from consideration. This should have indicated claims 2-8, 10 and 12-43 instead.

### ***Status of Claim Rejections - 35 USC § 102***

In the previous Office action, claim 1 was finally rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/30053 (Gordon et al).

In view of the present amendment to claim 1, the rejection is hereby withdrawn. Compounds from Gordon et al are no longer embraced by instant claim 1 because the R<sup>3</sup> group cannot be a simple alkyl group as in the reference compound from Gordon et al.

### ***Status of Double Patenting Rejection***

In the previous Office action, claim 1 was provisionally rejected under the doctrine of obviousness-type double patenting ("ODP") as being unpatentable over claims 2-21 of copending application serial number 10/333,556. Copending application serial number 10/333,556 discloses the elected species in the instant application, at page 200, as the compound "8" in the table on that page.

The terminal disclaimer filed on 5 April 2006, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on said copending application has been reviewed and is accepted. The terminal disclaimer has been recorded. Thus, the ODP rejection is hereby withdrawn.

***New Double Patenting Rejection***

Basis for the nonstatutory double patenting rejection comes from judicially created doctrine, and was explained in the previous Office action, pages 4 and 5.

Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2 and 3 of U.S. Patent No. 6,852,725 (to Thuriereau et al). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 2 and 3 of the patent are independent claims, drawn to single species, which species anticipate instant claim 1. In other words, instant claim 1 embraces the compounds to which claims 2 and 3 of the patent are drawn.

Claims 2 and 3 of the patent are drawn to compounds according to instant claim 1 wherein  $R^5$  is phenyl;  $R^1$  is hydrogen;  $R^2$  and  $R^6$  are hydrogen;  $R^4-(CH_2)_m-A^1$ ,  $A^1$  being  $-C(=Y)-N(X^1X^2)$ , wherein Y is O,  $X^1$  is either H (claim 3) or  $-(CH_2)_m-N-di-(C_1-C_6)alkyl$  (claim 2),  $X^2$  is  $-(CH_2)_m-Y^1-X^3$  with  $Y^1$  being a bond and  $X^3$  being a nitro-substituted  $-(CH_2)_m$ -phenyl moiety (claim 3) or a substituted  $(C_1-C_{12})alkyl$ , the substitution being  $-(CH_2)_mphenyl$ ;  $R^3$  is indol-3-yl- $(CH_2)-$  (claim 3) or  $-(CH_2)_4-NH-CO-O-t-Bu$ .

Applicants may opine that any double patenting rejection of the instant claims over claims of the patent which issued from the parent application, which patent is the patent serving as the basis for the double patenting rejection being set forth here, would be improper. The examiner would respond by pointing out that the prohibition on double patenting of claims in a divisional application over claims of the patent which issued from the parent application only applies when the claims in the child application

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are drawn to subject matter which was *restricted out* of the parent application. That is not the case here – instant claim 1 still embraces subject matter from the parent application, and in the prosecution of the parent application, a Requirement for Restriction was issued, to which Requirement, applicants responded by electing the compounds wherein “R1 and R2 do not form a ring, A1 is C(=Y) -NX<sup>1</sup>X<sup>2</sup>, and R3 is – CH<sub>2</sub>-indol-3-yl, and pharmaceutical compositions thereof” \*, the instant claims include, at least in part, that same subject matter.

***New Claim Rejection - 35 USC § 102***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by von Geldern et al, "Azole Endothelin Antagonists. 1. A Receptor Model Explains an Unusual Structure-Activity Profile" Journal of Medicinal Chemistry, vol. 39(4), pages 957-967 (1996).

On page 958 of von Geldern et al, an intermediate in the synthesis of the endothelin antagonists reported by the authors is described, having molecular structure diagrammed in structure number 8. The compound 8N, wherein X is NH, is a compound according to instant claim 1 wherein R<sup>1</sup> is a proton; R<sup>2</sup> is hydrogen; R<sup>3</sup> is – (CH<sub>2</sub>)-indol-3-yl; R<sup>4</sup> is –C(=Y)-X<sup>2</sup>, Y being O, X<sup>2</sup> being –(CH<sub>2</sub>)<sub>m</sub>-Y<sup>1</sup>-X<sup>3</sup>, with m=0, Y<sup>1</sup> is O, X<sup>3</sup> is optionally substituted alkyl, wherein the substituent is –(CH<sub>2</sub>)<sub>m</sub>-phenyl-X<sup>6</sup><sub>n</sub>, wherein m=0 and n=1 and X<sup>6</sup> is hydrogen. The “Cbz” in structure 8 of von Geldern et al is benzyloxycarbonyl (see page 964, last synthesis in column 1).

\*From the Reply under 37 C.F.R. 1.111, filed 17 September 2002, in application serial number 09/719,457 (the parent application).

***Allowable Subject Matter***

Claims 9 and 11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Compounds according to instant claims 9 and 11 are allowable over the prior art. The closest prior art with respect to claims 9 and 11 is the von Geldern et al reference, cited hereinabove in the rejection of claim 1 under 35 U.S.C. 102(b).

If, upon amendment, the instant claims are in allowable form, the subject matter of Group II as set forth in the Requirement for Restriction mailed 14 September 2004 will be rejoined, at which time said claims, will be the subject of a rejection under the first paragraph of 35 U.S.C. 112, for lack of a disclosure enabling the full scope of what is specified therein, if not amended.

In such a finding of lack of enablement, the examiner will rely on what is known by a physician of ordinary skill at the time the invention was made. The following reference provides some teaching as to what this level of skill was.

Emery et al, "Anti-Secretory properties of non-peptide somatostatin receptor agonists in isolated rat colon: luminal activity and possible interaction with p-glycoprotein" British Journal of Pharmacology, vol. 135, pages 1443-1448 (2002).

Applicants are invited to provide any additional material that they feel demonstrates the state of the art at the time the present invention was made with respect to the treatment of diseases and medical conditions with compounds having activity at the somatostatin receptor.

Emery et al teaches, generally, that treatment of diarrhea was understood to be a utility of somatostatin receptor agonists in 2002. Thus, it is not plausible to assert that

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treatment of, for example, acromegaly, Paget's disease, pancreatitis, cancers (all cancers, that is), panic attacks and GH-secreting adenomas (to name a few, all of which are specified in instant claim 34) with a somatostatin receptor agonist would have been understood by a physician of ordinary skill to be a utility of the compounds of the present invention at the time the invention was made.

In view of the teachings of Emery et al, the examiner submits that treatment of Crohn's disease, diarrhea, AIDS related diarrhea, chemotherapy related diarrhea, irritable bowel syndrome and watery diarrhea syndrome are enabled by the disclosure. Limitation of the claims of Group II subject matter to the treatment of these conditions will preclude any rejection under 35 U.S.C. 112, first paragraph, upon rejoinder and would allow the application to be passed to issue post-haste upon an amendment placing claims 1 , 9 and 11 in allowable form.

### **Conclusion**

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Tuesday-Thursday from 8:00am to 4:30pm or Monday from 6:00am to 1:30pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

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